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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/518,989

07/21/2005

Margaret Han Dugan

ON/4-32556A

7027

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7590

05/28/2008

NOVARTIS  
CORPORATE INTELLECTUAL PROPERTY  
ONE HEALTH PLAZA 104/3  
EAST HANOVER, NJ 07936-1080

EXAMINER

AULAKH, CHARANJIT

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

05/28/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/518,989	<b>Applicant(s)</b> DUGAN, MARGARET HAN	
	<b>Examiner</b> Charanjit S. Aulakh	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/21/06</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Applicants election of group II in paper filed on May 13, 2008 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse; see MPEP 818.03(a).

2. Claims 1-13 are pending in the application.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 5-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation

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necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

The specification merely mentions on page 1, 4<sup>th</sup> paragraph that anti-proliferative effect of a combination, which comprises a vasculostatic compound and an alkylating agent, is greater than the maximum effect that can be achieved with either type of ingredient alone. However, there is no teaching or guidance present regarding the specific compounds used or tumor cell line used in this combination. There is no teaching in the prior art showing synergistic effect of any alkylating agent in combination with any vasculostatic agent or instant compounds of formula I in any single known tumor cell line. There is lot of unpredictability regarding outcome of the combination treatment due to drug interaction. The combination of an alkylating agent may actually antagonize the anti-tumor effect of the instant compounds of formula I. There are no working examples present showing effect of combination using even a single vasculostatic compound and an alkylating agent in any tumor cell line. The instant compounds of formula I encompasses hundreds of thousands of compounds based on the values of variables A, B, D, E, G, Q, X, Y, n, m and r and alkylating agents and therefore, in absence of such teachings, guidance, unpredictability and presence of working examples, it would require undue experimentation to demonstrate the synergistic effect of instant compounds of formula I with thousands of alkylating agents in every known tumor cell line as compared to the either compound when used alone in the art and hence their utility for treating every known tumor or cancer in the art.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 5-8 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 5-8 and 10-13, the term ---tumor disease ---- is indefinite since specific diseases are not defined.

Claims 5 and 6 provide for the use of combination, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

#### ***Claim Rejections - 35 USC § 101***

7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 5 and 6 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

#### ***Claim Rejections - 35 USC § 102***

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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9. Claims 1-13 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Wood ( WO 02/41882 ).

Wood discloses combination comprising an agent decreasing VEGF activity and an agent decreasing EGF activity for treating tumors. The combination of vasculostatic agent, PTK787 and alkylating agent for treating proliferative disease disclosed in claims 9-11 and 14 by Wood clearly anticipate the instant claims.

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bold ( U.S. Patent 6,258,812, cited on applicants form 1449 ) in view of Reidenberg ( U.S. Patent 5,939,098 ).

Bold discloses anti-proliferative effect of phthalazine derivatives of formula I ( see col. 2, line 50 to col. 4, line 3) which are identical to instant compounds of formula I. Bold

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meets all the limitations of instant claims except that Bold does not exemplify using combination of phthalazine compounds with alkylating agents for anti-proliferative activity. However, Bold does teach combining phthalazine compounds with chemotherapy especially for treating tumors ( see column 11, lines 2-23 ) while Reidenberg teaches using temozolomide as a chemotherapeutic agent for treating numerous cancers ( see column 1, lines 40-65 as well as claims 1-12). Therefore, it would have been obvious to one skilled in the art to combine the compounds of Bold having different mechanism of action for anti-proliferative effect with temozolomide having different mechanism of action for anti-proliferative effect for treating tumors for obtaining synergistic effect of the combination treatment with reasonable expectation of success.

13. Claims 1-3, 5-9, 12 and 13 are objected for containing non-elected subject matter.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Charanjit S. Aulakh/  
Primary Examiner, Art Unit 1625